CERTIFICATE

This to certify that the dissertation entitled **"UTILITY OF CLINICALLY DIRECTED SELECTIVE SCREENING TO DIAGNOSE HIV INFECTION IN HOSPITALISED CHILDREN"** is a bonafide original work of **Dr. G.RAJKUMAR,** in partial fulfillment of the requirements for **M.D. Branch – VII (Pediatrics)** Examination of The Tamilnadu Dr.M.G.R Medical University to be held in March 2008.

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DECLARATION

I, **Dr. G.RAJKUMAR,** solemnly declare that dissertation titled, **"UTILITY OF CLINICALLY DIRECTED SELECTIVE SCREENING TO DIAGNOSE HIV INFECTION IN HOSPITALISED CHILDREN"** is a bonafide work done by me at Institute of Social Pediatrics ,Govt. Stanley Hospital during December 2005 to May 2007 under the guidance and supervision of my **Prof.Dr.SUJATHA SRITHARAN, M.D., D.C.H.,** Professor, Institute of Social Pediatrics, the dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University , towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – VII) in Pediatrics.**

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UTILITY OF CLINICALLY DIRECTED SELECTIVE SCREENING TO DIAGNOSE HIV INFECTION IN HOSPITALISED CHILDREN

Dissertation submitted to

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M.D. BRANCH - VII

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KEY TO MASTER CHART

F.occ	:	Father’s occupation
M.occ	:	Mother’s occupation
M.occ H W	:	House wife
HIV(F)	:	HIV status of father
HIV(M)	:	HIV status of mother
HIV(F) 0	:	not known
HIV(F) 1	:	Positive
HIV(M) 0	:	Not known
HIV(M) 1	:	Positive
PREV BT	:	History of previous blood transfusion
PREV BT 0	:	No
PREV BT 1	:	Yes
GLA	:	Generalized lymphadenopathy
HSM	:	Hepato spleenomegaly
PER.PNEU	:	Persistent pneumonia
M B I	:	Multiple bacterial infection
EP.TB	:	Extra pulmonary tuberculosis
FEVER	:	Fever for more than one month
COUGH	:	Chronic cough
CHR. DIARR.	:	Chronic diarrhea
WASTING	:	Wasting syndrome
ORAL THR	:	Oral thrush
R B I	:	Recurrent bacterial infection
GEN DER	:	Generalized dermatitis
SYMPTOM 0	:	Absent
SYMPTOM 1	:	Present
ELISA STATUS 1	:	Positive
ELISA STATUS 2	:	Negative

ABBREVIATIONS

HIV	:	Human immunodeficiency virus
AIDS	:	Acquired Immuno Deficiency Syndrome
L I P	:	Lymphoid Interstitial Pneumonia
P C P	:	Pneumocystis Carinii Pneumonia
ELISA	:	Enzyme Linked Immuno Sorbent Assay
PCR	:	Polymerised Chain Reaction
BAL	:	Broncho Alveolar Lavage
ART	:	Anti retroviral therapy
ARI	:	Acute respiratory tract infection
CDC	:	Centre for disease control
MAI	:	Mycobacterium avium intracellulare
WHO	:	World health organisation

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PROFORMA

Name:

Age / sex:

Address:

Father’s education, occupation,income:

Mother’s education, occupation,income:

Socio – economic status:

Mother’s HIV status known / not:

If known, took treatment / not:

Father’s HIV status known / not:

Previous history of blood transfusion:

History of early neonatal death of unknown etiology:

COORDINATES OF THE CURVE

Test Result Variable(s): age

Positive if Greater Than or Equal To(a)	Sensitivity	1 - Specificity
2.00	1.000	1.000
3.50	.983	1.000
4.50	.922	1.000
5.50	.914	1.000
6.50	.862	.917
7.50	.845	.917
8.50	.836	.833
9.50	.802	.833
11.00	.793	.833
13.50	.750	.833
16.50	.733	.833
21.00	.664	.667
27.00	.586	.667
31.00	.569	.417
34.00	.560	.417
39.00	.466	.333
45.00	.466	.250
50.00	.336	.167
53.00	.328	.167
57.00	.319	.167
63.00	.293	.167
69.00	.284	.167
78.00	.207	.083
87.00	.181	.083
93.00	.164	.083
102.00	.112	.083
114.00	.069	.083
126.00	.026	.000
138.00	.009	.000
145.00	.000	.000

INTRODUCTION

Children of today are youth of tomorrow. If we allow the HIV / AIDS epidemic to slowly but surely wipe away this precious generation from the face of the earth, we are going to be sorry in the future. This will impact our nation, continent and the world at large. It will adversely affect the health statistics, the economic growth and above all the morale of nations. As on today approximately 40 million people live with HIV infection worldwide of which one third are aged between 15 to 24 years. More than 90% of these patients live in developing countries that neither have adequate resources nor the required infrastructure to tackle this problem[1].

Today India has approximately 4 million people living with HIV infection. Six states namely, Maharashtra, TamilNadu, Andhra Pradesh, Karnataka, Manipur and Nagaland are high prevalence states. They have more than 1% seroprevalence of HIV infection among pregnant women attending antenatal clinic. These states are doing relatively well in their childhood health statistics at present. However HIV related mortality could upset all gains achieved in last couple of decades with efforts like promotion of breastfeeding, ARI control programme, diarrhea control programme, immunization, etc[1].

Twenty eight million deliveries occur in India annually. The average HIV prevalence in these pregnant women is 0.5%. This means 1.4 lakh deliveries occur in HIV infected women. Without any intervention, 30 % of these HIV infected women transmit HIV to their babies. It means 40,000 babies are HIV infected vertically in India annually[1]. Pediatric AIDS constitutes 2 %

of all HIV infected cases in developed countries as compared to 15 – 20 % in developing countries. In India women and children constitutes 50 % of all HIV infected patients.

The diagnostic procedures for HIV are not available at all centers and needs pre test and post test counseling.

The present study aims to find the utility of clinically directed selective screening to diagnose HIV infection in hospitalized children.

REVIEW OF LITERATURE

MODES OF TRANSMISION

Most of the HIV infections in children are vertically transmitted i.e. acquired from mothers. Blood and blood products, however, remain an important source and are responsible for infection in 10 % – 30 % of total cases in the developing countries[2]. Some of the mothers also acquire HIV through blood transfusion and transmit the infection to their babies[3].

HIV EXPOSURE IN INFANTS AND YOUNG CHILDREN

Mother to child transmission (MTCT) is by far the most significant route of transmission of HIV infection in children below the age of 15 years. In 2005 alone, 700,000 children were reported to have acquired HIV infection[4]. HIV can be transmitted during pregnancy, during child birth or breastfeeding. Without intervention, the risk of transmission from an infected mother to her child ranges from 15 % - 25 % in developed countries and from 25 % - 45 % in developing countries. This difference is largely attributed to breast feeding practices.

Estimated risk and timing of MTCT in the absence of intervention {Adapted from ***Kevin De Cock paper***}:

During pregnancy (5 – 10 %), during labour and delivery (10 – 15 %), during breast feeding (5 – 20 %), overall without breast feeding (15 – 25 %), overall with breast feeding to 6 months (20 – 35 %), overall with breast feeding to 18 – 24 months (30 – 45 %).

NATURAL HISTORY OF VERTICALLY TRANSMITTED HIV INFECTION

The clinical course of vertical HIV–1 infection is highly variable, but before the widespread use of antiretroviral therapy, two general patterns of survival were described. Approximately 10 – 20 % of infants experienced rapid progression of disease and died of AIDS related complication by 4 years of age. The mean survival time for the remaining 80 – 90 % infected children was approximately 9 to 10 years[5].

In a cohort of infants followed from birth, by 12 months of age 83 % had shown some sign of HIV disease, 74 % had progressed to category A, 55 % to category B, 21 % to category C and 6% to death[6.] Hepatomegaly and Lymphadenopathy were the most common category A signs during the first 6 months of life.

In another cohort study, category C events or deaths were estimated for 20 % of perinatally infected infants in the first year of life, with approximately 5 % succumbing per year thereafter[7].

Analysis of data from pediatric spectrum of disease project in the USA showed that the mean time spent by perinatally infected children in each stage were: N,10 months; A,4 months; B,65 months; and C,34 months[5]. In this study, it was estimated that a child born with HIV infection had a 50 % chance of severe signs or symptoms by 5 years of age, and a 75% chance of surviving to 5 years of age. The estimated mean time from birth to stage C was 6.6 years, and the estimated mean survival time was 9.4 years. This study highlighted that

perinatally infected children progress to moderate symptoms in the second year of life and then remain moderately symptomatic for more than half of their expected life span. This clearly underscores the need for their clinical care before the onset of AIDS.

In an African study, the estimated risk of death among perinatally infected children at 2 and 5 years of age was 45 % and 62 % respectively; median survival time was 12.4 months[8]. This study observed that early infection, early onset of HIV related conditions , failure to thrive and generalized lymphadenopathy were associated with subsequent risk of death, whereas, LIP was predictive of a milder illness. Thus the prognosis appears to be poorer in the African children.

There is no Indian data to describe the natural history of HIV infection in Indian children.

CLINICAL MANIFESTATIONS

Clinical manifestations depend on the severity of immunosuppression. These, in the initial stages may be non-specific and consists of failure to thrive, recurrent fever, diarrhoea and respiratory infections. Children may have hepatosplenomegaly, lymphadenopathy, neurological manifestations and recurrent bacterial infections. In contrast to adults, who present more frequently with distinct HIV associated conditions, infected children in developing countries present with a disease spectrum that is similar to uninfected children[3].

The centre for disease control and prevention (CDC), USA has classified clinical features of pediatric HIV infection into four clinical categories for children below 13 years of age[9]. Once classified, a child cannot be reclassified into a less severe category even if the child's clinical status improves such as in case of immune reconstitution following institution of ART or resolution of clinical event.

1. Category N, describes asymptomatic children without signs of symptoms is considered to be the result of HIV infection or who have only one of the condition listed in Category A.

2. Category A: children classified as category A should have two or more mild symptoms of HIV–related conditions such as : lymphadenopathy, hepatomegaly, splenomegaly, dermatitis, parotitis, recurrent upper respiratory tract infection such as sinusitis,otitis media etc., children with category B or C clinical conditions do not remain in category A even if they have multiple Category A conditions.

3. Category B defines children who are moderately symptomatic with HIV – related conditions. These include anemia, thrombocytopenia or nuetropenia persisting for more than 30 days; single episode of bacterial meningitis, pneumonia, or sepsis; CMV infection before one month of age; hepatitis; chronic diarrhea; lymphoid interstitial pneumonia (LIP);disseminated varicella zoster virus infections. Inclusion in category B can occur only in the absence of category C conditions.

4. Category C conditions, with exception of LIP,are AIDS defining conditions. These include, recurrent severe bacterial infections (meningitis, pneumonia, or sepsis), esophageal or pulmonary candidiasis, CMV disease at greater than one month of age, disseminated or extra pulmonary mycobacterium tuberculosis, pneumcystis carinii pneumonia, HIV encephalopathy.

This classification system provides a useful guideline for pediatricians to evaluate HIV progression in children. In addition, it serves as a standard for researchers worldwide to measure the importance of clinical events and in drug trials.

Apart from clinical manifestations the severity of illness can be assessed by CD4 counts in blood[9]. Lymphocyte counts and their subgroups depend on age and cut off values are different from adults. Status of immunologic function based on CD4 counts according to age is depicted in table below.

Immunological categories	**Age of the child**		
	<12 months	**1 – 5 years**	**6 – 12 years**
	Cells / mm^3 %	**Cells / mm^3 %**	**Cells / mm^3 %**
No evidence of suppression	≥ 1500 ≥ 25	≥ 1000 ≥ 25	≥ 500 ≥ 25
Moderate suppression	750 – 1499 15 - 24	500 – 999 15 - 24	200 – 499 15 - 24
Severe suppression	<750 <15	<500 <15	<200 <15

RECURRENT BACTERIAL INFECTIONS [10,11]

There is failure of both cell mediated and humoral immunity. Despite hypergammaglobulinemia, these children are at risk of severe and recurrent bacterial infection. There is delay in clearing of infections caused by the usual pathogens. Serious bacterial infections include bacteremia, meningitis, pneumonia, osteomyelitis, septic arthritis, and abscess at various sites.

Bacteremia is the most common clinically diagnosed sever bacterial infection. In various Indian studies, up to 90% of HIV infected children had history of recurrent pneumonias. Initial episodes of pneumonia often occur before the development of significant immunosuppression. As the immunosuppression increases, the frequency increases. The common pathogens for community acquired pneumonia in these children are streptococcus pneumoniae, H.influenzae, staph.aureus. However children with severe immunosuppression and in hospital acquired infections, gram negative organisms, such as, pseudomonas aeruginosa gain importance. The clinical features of pneumonia in HIV infected children are similar to those in uninfected children. However, in severely immunocompromised children, signs may be subtle. Often, the response to therapy is slow and the relapse rates are high. Bacteremia may be more common, seen in upto 50 %.

Sinusitis is the second most common clinically diagnosed bacterial infection in HIV infected children. A history of nasal discharge and persistent cough for more than 2 weeks should prompt suspicion of sinusitis in HIV infected children. The prevalence of meningitis, osteomyelitis, septic arthritis,

pericarditis and cellulitis does not appear to be unusually high. The pathogens and clinical symptoms are similar to immunocompetent children.

TUBERCULOSIS [12,13]

With the spread of the HIV infection, there has been resurgence in tuberculosis. The two diseases have significantly detrimental interactions. Co-existent TB and HIV infections accelerate the progression of both the diseases. HIV infection increases the susceptibility to primary infection, as well as to reactivation of tuberculosis infection due to depressed cell mediated immunity. Children at all stages of HIV infection can develop this infection [14,15]. In turn, active tuberculosis accelerates the progression of HIV disease. Tuberculosis causes activation of cytokines like TNF. Increased elaboration of cytokines and increased stimulation and enhanced multiplication of lymphocyte increases HIV replication and plasma HIV - RNA levels[16]. HIV infected children are more likely to have extra pulmonary and disseminated tuberculosis, the course is also likely to be rapid. An HIV infected child with tubercular infection is more likely to develop the disease than a seronegative child. The overall relative risk of active of active TB in children infected with HIV is at least 5–10 fold higher than in children not infected with HIV. In the absence if significant immunosuppression,the clinical manifestations are not much different from that in seronegative children. In patients with lower CD4 counts, the pulmonary lesions are more extensive. Mediastinal adenopathy is also more frequently seen. Pleural effusions are uncommon. Diagnosis of TB in infected children poses greater challenge than in other children. Even with the use of a lower cut off of 5 mm, the tuberculin test is often negative, particularly in

children with immunosuppression. The incidence of MDR TB is higher in HIV infected children.

MYCOBACTERIUM AVIUM – INTRACELLULARE INFECTION (MAI) [14]

Pulmonary disease with MAI is uncommon in children with HIV infection despite immunosuppression.

The common symptoms and signs include: Persistent fever, failure to thrive, night sweats, lymphadenopathy, organomegaly, and refractory anemia. The pulmonary lesions are usually limited to lymphadenopathy and localized parenchymal lesions. The diagnosis of disseminated disease primarily depends on isolation of the organism from blood. Current therapy for disseminated MAI infection includes clarithromycin or azithromycin with ethambutol.

PNEUMOCYSTIS CARINII PNEUMONIA[14,17,]

PCP is the most common opportunistic infection in HIV infected children. However, there is lack of data from India to define the magnitude of the problem. The data from Africa show a low incidence of PCP. Children with PCP are sicker than adults with this infection with high case fatality rate. In 1992, the estimated median survival after diagnosis of PCP was 19 months. Onset is acute in infants while older children have a more indolent and protracted course. The clinical features are tachypnoea, dyspnoea and fever. The examination of chest is unremarkable except for tachypnoea and chest retractions. Chest radiograph shows diffuse interstitial lung disease without

hilar adenopathy. Other patterns include localized infiltrates, hyperinflation, and non cardiogenic pulmonary edema. The radiograph may be normal in less than 5% children. Hypoxemia is the hallmark of PCP. A markedly elevated (A-a) DO_2 and a high serum LDH levels are often seen.

The diagnosis of PCP begins with suspicion. The diagnosis requires demonstration of cysts or organisms in lung secretions or tissue. Induced sputum, nasopharyngeal swab, and BAL are feasible techniques to detect PCP. Stains like Giemsa stain (for organism), Gomori stain, toluidine blue Ostain (for cyst wall) are used. PCR has also been used for detecting organisms in respiratory secretions.

VIRAL INFECTIONS[14]

In children with AIDS, disseminated CMV is a known opportunistic infection, but pneumonia is rare. Prospective data showed that when HIV infected children develop RSV virus disease, they are less likely to wheeze and more likely to have pneumonia and prolonged shedding of virus. Infections with influenza, herpes simplex and varicella virus have been reported but are uncommon.

FUNGAL INFECTIONS [14]

Fungal infections especially invasive infections are also seen more frequently. These include candidiasis, cryptococcosis, histoplasmosis and aspergillosis. Mucosal and cutaneous fungal infections are more commonly seen than systemic infections. Most HIV infected children develop oral

candidiasis at least once. These children are also at increased risk of oesophageal candidiasis. Pulmonary fungal infections usually present as a part of disseminated disease in immunocompromised children. Primary pulmonary fungal infections are uncommon. Pulmonary candidiasis should be suspected in any sick HIV infected child with lower respiratory tract infection that does not respond to common therapeutic modalities.

Aspergillosis is an uncommon infection in HIV infected children. Invasive disease is common in these children as persistent pneumonia associated with atelectatic or large apical cavitatory lesions. Pneumothorax is common. The diagnosis of invasive bronchopulmonary aspergillosis must be considered in a child with compatible clinico-radiologic picture and recovery of organisms in pure culture from BAL, if other causes are excluded. In children with advanced HIV infection, the disease runs an aggressive course.

Cryptococcosis commonly presents as a subacute meningitis or meningoencephalitis; many children may present with nonspecific, subtle symptoms, including fever and headache. Pulmonary involvement may be seen in half of these children. However, isolated pulmonary cryptococcosis is not commonly seen. Other uncommonly reported fungal infections include histoplasmosis and coccidioidomycosis.

LYMPHOID INTERSTESTITIAL PNEUMONIA (LIP)[18]

LIP has been recognized as a distinctive marker of pediatric HIV infection and is included as a Class B condition in revised CDC criteria for AIDS in children. While the prevalence in HIV infected children in the west

has been reported to be around 20%, figures from Africa suggest that it is not common. The etiology and pathogenesis of LIP are not well understood. Suggested etiologies include: an exaggerated immunological response to inhaled or circulating antigens, and/or primary infection of lung with HIV or Ebstein Barr virus or both. There is evidence to suggest that EBV plays significant pathological role in LIP.LIP is considered to reflect a local response to persistent antigenic stimulus that could be EBV, which is a potent polyclonal stimulator for B cells.

LIP is more common in children with perinatally acquired HIV infection than in children who acquire HIV infection in the other ways. This may be due to direct intrauterine or intrapartum exposure of lung tissue to HIV. LIP is characterized by nodule formation and diffuse infiltration of the alveolar septae by lymphocytes, plasmacytoid lymphocytes,plasma cells and immunoblasts. There is no involvement of blood vessels or destruction of lung tissue. Children with LIP have a relatively good prognosis compared to other children who meet CDC surveillance of AIDS. LIP is usually diagnosed in children with perinatally acquired infection when they are older than a year of age in contrast to PCP diagnosed typically in the first year of life.

The presence of reticulonodular pattern, with or without hilar lymphadenopathy, that persists on chest radiograph for 2 months or greater and that is unresponsive to antimicroboial therapy is considered presumptive evidence of LIP.

DIARRHOEA[19,20]

Diarrhoea – acute,recurrent and persistent – is a common infection in HIV infected children. In a HIV child, infection with any enteropathogen can result in prolonged diarrhea and malabsorption with subsequent malnutrition. The etiological agents for diarrhoea include the common enteropathogens, C.jejuni, Helicobacter cinaedi, shigella and cryptosporidium.

Cryptosporidium is associated with voluminous profuse watery diarrhea,anorexia,weight loss and even death in HIV infected individuals. Stool contains mucus but no blood or leucocytes. The risk of persistent diarrhea is increased with cryptosporidium infection. Diarrhea may also be due to systemic infection with atypical mycobacteria , CMV, HIV enteropathy, drugs or bacterial overgrowth.

HIV ENCEPHALOPATHY [18,21]

HIV -1 associated neurological disease known as *"HIV -1 associated progressive encephalopathy"* is a common concomitant in the progression towards AIDS. It is characterized by a triad of symptoms including impaired brain growth, progressive motor dysfunction, and loss or plateau of developmental milestones is believed to result from both direct and indirect effects of HIV infection. Consequent to the hallmark systemic immunedeficiency of HIV infection , the CNS becomes susceptible to opportunistic infections, which add further morbidity and mortality and may contribute either directly or indirectly to neurological symptoms which can often mimic progressive encephalopathy.

Static encephalopathies represent fixed, nonprogressive neurological or neuro developmental deficits in HIV infected children. It may or may not be caused by HIV infection but are often associated with such identifiable insults as prematurity, in utero exposure to toxins or infectious agents or head trauma.

ORAL MANIFESTATIONS[22]

Oral manifestations are directly related to degree of immunosuppression and such lesions can be considered as indicators of the progression of HIV infection in children.

Santosh L.C et al,involving 80 HIV infected children (average age of 6.3 ± 3.2years) , 30 (38 %) had some type of oral lesions; the CD4 counts were lower than that found in lesion free children. Common lesions include candidiasis (22.5 %) ,gingivitis (17.5 %) , enlargement of parotids (8.8 %) , herpes simplex (1.3 %), and hairy leukoplakia (1.3 %)

HEMATOLOGICAL MANIFESTATIONS [18]

Hematological manifestations in pediatric HIV infection include anemia, neutropenia, absolute or relative lymphopenia, thrombocytopenia and eosinophilia. Severe thrombocytopenia and anemia are correlated with poor prognosis. These abnormalities may occur because of peripheral destruction of blood elements, HIV replication, poor nutritional status and adverse effects of medications.

CARDIOMYOPATHY [24]

Cardiovascular problems associated with infection including left ventricular dysfunction and increased left ventricular mass are common and clinically important indicators of survival for children infected with HIV. A prospective multicenter cohort study has evaluated 205 vertically HIV – infected children enrolled at a median age of 1.9 years, 600 HIV – exposed children enrolled prenatally or as neonates, of whom 93 were ultimately HIV – infected. The main outcome measures were echocardiographic indices of left ventricular dysfunction. Left ventricular dilatation, heart failure, and / or the use of cardiac medications were more common in infected compared with uninfected children. The mortality rate 1 year after the diagnosis of heart failure was 52.5% (95% CI, 30.5 – 74.5). Authors concluded that cardiac dysfunction occurred in 18% to 39% of HIV – infected children and was associated with an increased risk of death. They have recommended that HIV – infected children should undergo routine echocardiographic surveillance for cardiac abnormalities. Zidovudine induced cardiomyopathy has also been reported.

RHEUMATOLOGICAL MANIFESTATIONS[23]

Rheumatological manifestations are uncommon in HIV–infected children. In one study [23], these were identified in 5 (19.2 %) out of 26 children. These included biphasic Reynaud's syndrome,necrotizing vasculitis, lip necrosis, livedi reticularis, knee arthralgia, vasculitis, and septic arthritis of ankle. All of the rheumatological manifestations were seen in advanced stage

of HIV disease. These rheumatological changes were similar to those reported for HIV- positive adults.

OTHER MANIFESTATIONS [14,18]

HIV – infected children also suffer from various infectious and non-infectious conditions of the skin. Non infectious conditions include seborrhoeic dermatitis, atopic dermatitis, eczema, drug eruptions and skin lesions associated with nutritional deficiencies. Up to 10% of HIV-infected children may have nephropathy. This may manifest with hematuria, proteinuria, renal tubular acidosis, and acute renal failure. These manifestations are common with advanced disease. Majority of HIV – infected children suffer from nutritional and growth abnormalities.

Growth retardation in HIV infected infants is evident as early as 4 – 6 months of age. HIV infection or associated opportunistic growth first affects linear growth. Overall effect on height for age is more than weight for age. Early growth delay has been correlated with viral load. In addition, recurrent infections, decreased oral intake because of oral and esophageal lesions and various organ dysfunctions also contribute to failure to thrive.

Hepatomegaly is the common clinical manifestation of pediatric HIV disease. Histopathological findings in liver include: fatty infiltration of hepatocytes, portal inflammation, CMV inclusion bodies and giant cell transformation and chronic active hepatitis characterized by lymphocytic infiltration in portal spaces and lobules.

Lymphadenopathy is seen in infants and children with HIV. Generalized lymphadenopathy may be because of HIV infection, other viral infections (Ebstein Barr virus or CMV), opportunistic infections and malignancies (lymphoma / leukemia).

The prevalence of malignancies in HIV infected children is believed to be significantly higher than in normal population. The common malignancies reported in HIV infected children include: non Hodgkin's lymphoma, leiomyosarcoma or leiomyoma, leukemia, kaposi's sarcoma, Hodgkin's lymphoma, vaginal carcinoma in situ and tracheal neuroendocrine carcinoma.

CLINICAL CASE DEFINITION OF HIV INFECTION

Since majority of infections are acquired vertically, the best method for identification of HIV infection should be to screen all mothers and suspect HIV in babies born to HIV positive mothers. Since screening of mothers for HIV is not done universally and some patients get HIV infection through transfusion of blood and blood products, we may see children with clinical manifestations of HIV in majority.

Because of the limited availability of HIV diagnostic testing, attempts have been made to formulate clinical AIDS definitions for adults and children in developing countries. Use of the Centre for Disease Control and Prevention (CDC) guidelines for clinical classification of HIV infection in children is problematic because they were designed to measure HIV disease progression, not for the identification of children infected with HIV. In addition, many

category C (or AIDS) diagnoses are beyond the diagnostic capabilities of most of the developing world.

Several simple clinical case definitions pertinent to the developing world have been devised and tested, including the WHO clinical case definition[25]. These definitions detect the presence of symptomatic AIDS and not HIV infection itself and are confounded by prevalent conditions such as malnutrition, diarrhoeal disease and tuberculosis. There are no published studies in literature to test the sensitivity and specificity of WHO's modified criteria in Indian patients. The reported[26,27] sensitivity of individual factors including weight loss or failure to thrive is 45–100%, chronic diarrhea (>1 month) 15 – 45 %, and severe or repeated pneumonia 8 – 86%. For minor criteria such as generalized lymphadenopathy is 23 – 41% and for oro-pharyngeal candidiasis 14 – 48%. The wide variations in sensitivity is due to different clinical settings. The published studies do not mention about the sensitivity of two major signs associated with at least two minor signs.

One should suspect HIV infection in a child who presents with symptoms described in category C of CDC, has specific illness like LIP, has atypical manifestations of common illnesses, presents with combinations of symptoms or born to HIV positive parents.

CLINICAL CASE DEFINITIONS OF PEDIATRIC AIDS

Modified WHO Criteria for case definition for pediatric AIDS

Major criteria	**Minor criteria**
Weight loss or failure to thrive	Generalized lymphadenopathy
Chronic diarrhea (> 1 month)	Oropharyngeal candidiasis
Prolonged fever (> 1 month)	Repeated common infections
Severe or repeated pneumonia	
Generalized dermatitis	
Confirmed maternal infection	

Pediatric AIDS is suspected in an infant or child presenting with at least two major signs associated with at least two minor signs in the absence of known causes of immunosuppression.

STRATEGIES OF HIV TESTING [28]

Various categories of tests are used in combinations

i. ELISA / Simple / Rapid /, Elisa / Rapid / Simple used in category I,II

ii. Supplemental tests like Western Blot, Line immunoassay are used in problem cases or when results are indeterminate.

Strategy I

Serum is subjected to one E / R/ S for HIV. If negative, it is to be considered free of HIV and if positive the sample is taken as positive. This method is used for ensuring donation safety.

Strategy II

A serum is considered negative if the first ELISA is negative. If reactive it is subjected to a second ELISA which utilizes a different system from the first one. It is reported reactive only if the second test confirms the results of the first. This strategy is used for surveillance and diagnosis only if some indicator of the disease is present.

Strategy III

It is similar to the above strategy II with the addition of a third reactive ELISA being required for a sample to be considered as positive. The test for the first ELISA should have high sensitivity and for the second and third ELISA high specificity. It is used to diagnose infection in asymptomatic individuals.

Testing for HIV infection involves aspects of pretest counselling, explicit consent and confidentiality. Laboratory safety must be strictly followed according to Good Laboratory Practice(GLP) guidelines and universal precautions must be observed.

Types of tests available are

1. Anti HIV antibody tests,
2. Virus based tests,
3. Immunological tests and
4. Surrogate markers.

Specimens used to test for HIV infection

1. **Antibody detection**: blood, serum / plasma.
2. **Antigen detection**: serum / plasma, CSF, Cell culture supernatant
3. Virus isolation and detection of viral nucleic acids:

Plasma, semen, vaginal / cervical specimens, CSF.

Less successful – saliva, urine, breast milk, tears and amniotic fluid.

Anti HIV antibody tests:

There are two categories:

1. Screening tests
2. Supplemental tests

I. SCREENING TESTS

a. Conventional micro well ELISA tests

b. Rapid tests

Screening tests employed should test antibodies to both HIV 1 and HIV 2 and their subtypes including O and N.

b. ELISA (Enzyme linked immunosorbent assay)

This is the most commonly performed test to detect HIV antibodies.

Types of ELISA based on the principle

1. Indirect ELISA
2. Direct ELISA
3 Competitive ELISA
4. Antigen sandwich and
5. Antigen antibody capture assay.

Types of ELISA based on antigen utilized

1. First - infected cell lysate
2. Second - recombinant glycoprotein
3. Third - synthetic peptidase

ELISA can take up to 3 hrs to yield results.

a. Rapid tests

They give results within minutes (3 – 30 minutes). Various rapid tests available are –

1. Dot blot assays
2. Particle agglutination (gelatin, RBC, latex, micro beads)
3. HIV spot and Coomb's tests
4. Fluorometric microparticle technologies

i. Supplemental Tests

These tests are used if the results of the screening tests are discordant and for research purposes. Otherwise according to the WHO guidelines, an individual reactive to three different systems of ELISA or rapid tests can be labeled to be having HIV infection.

These tests also identify and differentiate infections by HIV - 1 and HIV– 2.

These tests include –

Western Blot (WB), Line immunoassay (LIA), Recombinant Immunoblotting assay (RIBA)

Western Blot analysis is done by electrophoresis if plasma on a pre – impregnated strip containing various antigens of HIV. WB is interpreted as positive if at least 2 or 3 bands (p 24, gp 41, gp 120/160) are positive.

Direct detection of HIV

Direct detection of virus would be needed in the following settings –

For diagnosis

HIV infection in the newborn, Indeterminate WB / LIA / RIBA results, Monitor viral load during antiretroviral therapy, HIV infection status during window period, Detection of site specific infection

For research

Subtyping of HIV

Cloning genes for diagnosi\tic kits / vaccines,Generating chimeric virus

Techniques used:

1. Detection of p24 antigen
2. Culture isolates of HIV
3. Detection of HIV specific DNA or RNA Polymerase Chain Reaction (PCR)

HIV p24 core antigen

HIV p24 antigen is detected and quantified using EIA. Specificity and sensitivity reported are 79 % and 99% respectively. It correlates well with the disease progression. P24 is undetectable in most asymptomatic patients and infants. It also shows poor intrasample reproducibility. All these factors limit the utility of p24 assay.

Immune complex dissociated (ICD) p24 antigen

p24 antigen dissociated from the immune complexes improves the sensitivity of the assay. However, the sensitivity level is sub optimal for early diagnosis of HIV infection.

HIV isolation by viral culture

This requires at least P 2+ containment facility and high degree of expertise. Autologous or heterologous peripheral blood mononuclear cells

(PBMCs) activated with mitogen are co cultured with infectious material at 37ºC in 5% CO_2 for about 28 days. The presence of the virus is detected by presence of p24 antigen or reverse transcriptase enzyme in the culture supernatant. This method has the sensitivity and specificity of PCR, however it is costly, labor intensive and takes 2 to 4 weeks.

Polymerase chain reaction (PCR) for HIV

HIV DNA PCR (Qualitative)

This detects proviral DNA that is integrated with the host cell. This is best done using Reverse Transcriptase (RT) PCR. Because of the high sensitivity of the test, care is taken to avoid cross contamination of samples or carry over of amplified products.

HIV RNA PCR (Quantitative)

This is done using RT PCR or nucleic acid sequence based amplification (NASBA) and branched chain DNA (bDNA) techniques. Comparative analyses have shown that quantitative PCR studies are more sensitive measures of viral load than p24 assays and culture techniques at all stages of HIV infection, enabling detection of virus in plasma even when other assays are negative.

Laboratory diagnosis of HIV infection in the newborn (congenital infection)

The risk of mother to child transmission of HIV is 25 – 45%. Maternal IgG to HIV crosses the placenta and persists for 6 – 18 months. It is essential to

diagnose infections in newborns as early as possible. It relieves the parents' anxiety and is helpful to consider antiretroviral therapy in infected babies. PCP prophylaxis can be stopped if the baby is not infected. Early diagnosis also helps timely decisions regarding breast feeding, immunization etc. Distinction between maternal and neonatal IgG is difficult. The following tests can be used for early detection of congenital HIV infection:

1. Detection of Ig A and or Ig M anti HIV antibodies: Ig A antibodies appear at 3 – 4 months of age and Ig M by six months of age. Ig A after 3 months of age has a sensitivity of 97.6% and specificity of 99.7%. Ig M production is erratic and elicits false positive results.

2. Estimation of p24 antigens: this has high frequency of false positivity in the first month of life.

3. HIV DNA PCR, HIV RNA PCR and viral cultures: PCR is preferred over culture techniques. It invariably has a specificity of > 95%. The sensitivity ranges from 38% within 48 hrs of birth, to more than 93% at 14 days and 96% by 28 days of life.

Cord blood is not to be used for testing as there can be contamination. The negative ELISA done between 6 – 18 months in the absence of clinical disease will rule out HIV infection (in an infant who is not breast fed).

For infection in utero, the HIV DNA PCR or viral culture has to be positive in the first 48 hours. For intrapartum infection the tests within 48

hours are negative but positive after one week. If one PCR is to be done due t cost constraints then it is best performed between 3 to 6 months of age.

Reporting procedure

The results are kept confidential.

Negative – if the initial / screening test is nonreactive.

Positive – if the sample shows reactive results by three screening tests.

Indeterminate – if the sample shows discordant results by three screening tests. Confirmatory assay is to be done. If the confirmatory assay is indeterminate the following samples are tested at three, six and 12 months before the result is reported. If still indeterminate after one year, the person is declared negative.

In summary, to diagnose congenital HIV infection in early infancy ELISA is unreliable. The mainstay is by HIV PCR or rarely by viral culture. After 18 months of age three serial ELISAs can be done. The disease progress has to be monitored by assay of CD4 counts.

GENERAL MANAGEMENT OF HIV IN CHILDREN [29]

Early management of pediatric HIV disease is based on timely institution of chemoprophylaxis, immunization, management of opportunistic infections, nutritional support and anti retroviral therapy. However early management using appropriate measures are possible only if these children are

diagnosed early. Spectacular advancement has been made in strategies to reduce mother to child transmission. The vertical transmission of HIV infection may occur in utero (30 – 50%), intrapartum (50 – 70%), or through breast feeding (about 15%). Of the HIV infected children about 20 – 30% are rapid progressors. Among the slow progressors 15% are asymptomatic even at 5 years of age. The slow progressors reveal a lower rate of fall of absolute CD4counts. The median survival time of vertically infected children is reported to be 8 – 9 years. Plasma HIV RNA levels of more than 2, 99,000 copies per milliliter in an infant has been correlated with rapid progression of the disease and death. In general, plasma HIV RNA levels of more than 1,00,000 copies / ml and CD4 counts of < 15 % are considered as poor signs of survival.

Breast feeding

There is 14 – 16 % risk of mother to child transmission of HIV through breast milk. In a developing country like India where the breast feeding safeguards against risk for diarrhea and respiratory infections, which by themselves are associated with high mortality and morbidity, the risks from breastfeeding needs to be individualized. Whenever safe, cost effective and alternate source of milk are available, the HIV infected mother need to be counselled not to breast feed their infants. Mother and family participation in decision making is imperative.

Nutrition

Factors like repeated infections, poor intake, malabsorption, increased requirements and emotional deprivation make a HIV positive child more prone for malnutrition. Malnutrition itself can augment the immunodeficiency in HIV

infected children. The diet should consist of high calories, proteins and vitamins preferably from home made foods. Treatment of opportunistic infections, oropharyngeal and esophageal candidiasis, diarrhea and respiratory infections is necessary to help in keeping the oral intake adequate. Health education and economic support may be necessary for better nutrition. In extreme or terminal cases tube feeding or total parenteral therapy may become necessary for a short period of time. Emotional and psychological support for the family is essential.

Anti retroviral therapy

Three classes of anti retroviral therapies (ART) are available for HIV. Two of these target the reverse transcriptase enzyme, nucleoside (NRTI) and non-nucleoside (NNRTI) reverse transcriptase inhibitors. The third class of drug is a protease inhibitor which target the viral protease enzyme. Drug absorption, metabolism, pharmacokinetics and interactions should be understood well before undertaking therapy. Compliance is also difficult as the drugs are expensive and some are unpalatable. Treatment with ART needs proper patient selection, appropriate choice of drugs, monitoring and evaluation to look for need of change in treatment regimens.

Management of opportunistic infection

Prior to the use of ART in survival of HIV infected children were mainly due to chemoprophylaxis of opportunistic infections. Pneumocystis carinii pneumonia (PCP) is the most common infection seen in about a third of pediatric HIV infected patients and is an important clinical indicator of AIDS.

PCP prophylaxis is done using Trimethoprim – Sulphamethoxazole (TMP – SMX). Fungal infections are common in HIV / AIDS children. Oral or topical drugs are used in early cases and intravenous anti fungal agents in non-responders and in wide spread disease. Cryptococcal meningitis, CMV retinitis, varicella zoster, herpes simplex virus infection and measles are uncommon in children.

Monitoring growth and development

Anthropometric measurements at regular intervals are necessary for early recognition of growth failure and malnutrition. Height, weight, head circumference and skin fold thickness measurements can be used to predict disease progression and overall effectiveness of ART. Mental development should be monitored as it can be affected due to encephalopathy and opportunistic infections.

Counseling

Counseling to the patient and the family members should be an essential ongoing process throughout the course of the disease. The mother or the care giver should be counseled regarding diagnosis, treatment, follow up, prophylaxis against opportunistic infections, immunization, breastfeeding, prevention of transmission of HIV and socio-economic consequences of the infection.

Schooling

Children with HIV infection should not be excluded from school for the protection of other children and personnel since HIV does not spread through

the types of contact that may occur in school. The family of an affected child has the right, but not obliged to inform the school about the infection status of the child. All schools should adopt the standard procedures for handling blood or contaminated fluids regardless of the HIV status.

Home care

The family should follow standard guidelines to prevent exposure to HIV infected material. Sharing of toothbrushes, razors should be avoided. Hands and body parts should be readily washed after contact with blood. Routine changing of diapers and nose wipes should be followed by hand washing.

When blood or blood-contaminated fluids are spilled the surface should be cleaned and then disinfected with freshly prepared 1 :10 dilution household bleach.

Immunization

Immunization in the HIV positive chidlren differs from the routine as live vaccines are contraindicated with some exceptions. There may be a sub-optimal sero conversion after vaccination.

RECOMMENDATION FOR VACCINATION IN DEVELOPING COUNTRIES

VACCINE	RECOMMENDATION
BCG	Recommended by WHO, as tuberculosis is rampant and neonates are asymptomatic.
OPV	Ideally IPV should be given. Since it is not available OPV is recommended, as evidenced by absence of complications in those who were given OPV in early epidemics.
Measles, MMR	Measles and MMR vaccines are contraindicated only in children who are severely immunocompromised. (category C)
DPT,Hepatitis B,Hemophilus influenza type B	These vaccines are recommended because they do not contain any live agent. Hepatitis B immunoglobulin should be given within 7 days of exposure.
Varicella	Recommended only for the asymptomatic or mildly symptomatic (CDC classification N1 or A1 with an age specific CD4 of >25%). Immunoglobulin should be given within 4 days of exposure.
Pneumococcal	All HIV infected children who are 2 years or older should receive the vaccine, with a booster 5 years later.
Influenza	HIV positive children should receive yearly vaccine after 6 months of age.
Hepatitis A	Recommended for those living in endemic areas.
Typhoid	Vi polysaccharide vaccine is recommended. Oral typhoid vaccine is contraindicated.
Rabies	Vaccine and immunoglobulin can be given for post exposure prophylaxis.

AIM OF THE STUDY

To find the probability that child is sero positive for HIV when the child is admitted with at least one of the selected manifestations

MATERIALS AND METHODS

Type of study	:	Prospective study
Place of study	:	Institute of Social Pediatrics, Stanley Medical College & Hospitals.
Duration of study	:	December 2005 to May 2007.
Inclusion criteria	:	Any children who are admitted with any of the selected manifestations
Exclusion criteria	:	Any children who are already seropositive for HIV

Children aged 0 – 12 years admitted in Institute of Social Pediatrics, Stanley Medical College & Hospitals, were taken and among them who had any of the selected clinical manifestations suggestive of HIV were chosen as subjects. HIV serology was done after pre-test and post-test counseling (done by ICTC Counselors) and informed consent from them by ELISA method and for children below 18 months as the ELISA is not confirmatory they are subjected to detect HIV DNA if they are ELISA positive.

DEFINITION OF CLINICAL RISK FACTORS STUDIED

1. FEVER FOR MORE THAN A MONTH:

Documented fever (axillary temperature more than 37.8 ºC) over a month

2. CHRONIC DIARRHOEA

Presence of two or more loose stools per day for a period exceeding one month.

3. SEVERE MALNUTRITION

The presence of grade III protein energy malnutrition as defined by Gomez's classification, namely 60% or less of expected weight for the age using the fiftieth percentile of the NCHS standards as the reference

4. PERSISTANT PNEUMONIA

History of cough for more than one month

5. GENERALISED LYMPHADENOPATHY

Presence of enlarged lymph nodes(diameter of lymph nodes more than 1 cm in axilla and cervical region and more than 1.5 cm in inguinal region) in two or more non contiguous sites for more than 3 months.

6. ORAL THRUSH

Presence of whitish plaques in the oral cavity which could not be easily removed and when removed showed an erythematous base.

7. HEPATO SPLEENOMEGALY

Liver span more than 4 – 7 cm (depending upon patient's age) as detected clinically,moderate splenomegaly

8. REPEATED COMMON INFECTION

Two or more episodes of infections such as upper respiratory tract infections and gastroenteritis in the last 6 months.

9. GENERALISED DERMATITIS

Which includes eczema,disseminated maculopapular dermatoses.

10. CHRONIC PAROTID SWELLING

Swelling of at least one of the parotid glands for a minimum period of 3 months.

11. RECURRENT BACTERIAL INFECTIONS

Occurrence of more than two episodes of serious bacterial infections such as pyogenic meningitis and pneumonia in two years period.

Pyogenic meningitis. Diagnosed on the basis of clinical history , signs of meningeal irritation and results of CSF examination

Pneumonia: Diagnosed on the basis of clinical findings and results of radiological studies.

12. DISSEMINATED TUBERCULOSIS

Milliary tuberculosis {diagnosed on the basis of milliary mottling on the chest radiograph} or **CNS tuberculosis**: {diagnosed on the basis of CSF findings and / or results of neuroimaging studies in relevant clinical settings} or **Pulmonary tuberculosis** in conjugation with abdominal tuberculosis {diagnosed on the basis of results of radiological, bacteriological and cytological studies in clinically relevant settings}

13. PNEUMOCYSTIS CARINII PNEUMONIA

Diagnosed on the basis of clinical features{fever,cough,respiratory distress}, results of arterial blood gas analysis, findings on chest radiograph and microbiological studies.

OBSERVATION AND RESULTS

AGE AT PRESENTATION: (in months)

Mean	45.43
Std deviation	36.776
Minimum	3
Maximum	144

	Frequency	**Percent**
<1.5 yrs	43	33.6%
1.5 -5 yrs	49	38.3%
>5 yrs	36	28.1%

Age	**ELISA Status**			
	Negative		**Positive**	
	n	**Row %**	**n**	**Row %**
1.5 yrs	39	90.7	4	9.3%
1.5-5yrs	43	87.8	6	12.2%
>5yrs	34	94.4	2	5.6%
$X^2 = 1.09$, p =0.58, not significant				

In this study mean age at presentation of children with clinical manifestations was 45.4 months with maximum of 144 months and minimum of 3 months

Of 128 children included in our study, 33.6%(43) were <1.5 yrs, 38.3%(49) were 1.5-5 yrs , 28.1%(36) were >5 yrs.

SEX

Of 128 children 77 were male and 51 were female

Sex	**ELISA Status**		**Total**
	Negative	**Positive**	
Male	70	7	77
Female	46	5	51

X^2=1.09,p=0.89 not significant

Of 77 male children 7 were positive for elisa and of 51 female children 5 were positive for ELISA. There was no significant correlation between sex and seropositivity

OCCUPATION OF PARENTS

Mother's occupation

Among then128 children enrolled in the study 109 children's mothers were house wife 19 were working women all the mothers of children who were positive were housewife this was statistically significant

Mother	Elisa status		Total
	Negative	Positive	
House wife	97	12	109
Working women	19	0	19

$X^{2=6.46,}$ p =0.03 significant

Father's occupation

Among the fathers of children in the study 84 were daily wagers by occupation followed and masons, fishermen and tailors. Others were less in number.

Father's occupation	Elisa status		Total
	Negative	Positive	
Auto driver	1	0	1
Barber	1	0	1
Carpenter	1	0	1
Cooley	76	8	84
Farmer	3	1	4
Fisherman	5	0	5
Lorry driver	0	1	1
Mason	9	2	11
Painter	2	0	2
Rickshaw man	3	0	3
Salesman	1	0	1
Shop owner	2	0	2
Steel polisher	5	0	5
Tailor	6	0	6
Tea vendor	1	0	1
Total	116	12	128

We could not find any correlation between father's occupation and elisa positivity in children.

Elisa status of parents

HIV status of father was not known in 125 children and was positive in 3 children all the children who were positive were among children whose father's elisa status was not known

HIV status of father	Elisa status				Chi square
	Negative		Positive		X2=0.32
	n	%	n	%	p=0.57 not significant
No	113	97.4%	12	100%	
Yes	3	2.6%			

There was no correlation between father's ELISA status and HIV positivity in children

HIV status of mother was not known in 123 children and was positive in 5 children and all the children who were positive were among the 123.

HIV status of mother	Elisa status				Chi square
	Negative		Positive		
	n	%	n	%	X2=0.53
No	111	95.7%	12	100%	p=0.46 not significant
Yes	5	4.3%			

History of previous blood transfusion

In this study history of previous blood transfusion was negative in 126 children was positive in two One among the two was positive and it was statistically significant

H/O previous blood transfusion	Elisa status				Chi square
	Negative		Positive		
	n	%	n	%	X2=3.95
No	115	99.1%	11	91.7%	p=0.05 **significant**
Yes	1	0.9%	1	8.3%	

Risk factors for HIV

Among the selected manifestations suggestive of HIV in children oral thrush,generalized lymphadenopathy and wasting were significant risk factors for child being HIV positive in this study. Among 128 children 89 had no wasting and 39 had wasting and among the 89 who had no wasting 5 were positive and of 39 with wasting 7 were positive. This was statistically significant.

Wasting	Elisa status				Chi square
	Negative		Positive		
	n	%	n	%	X2=4.85
No	84	72.4%	5	41.7%	p=0.02 **Significant**
Yes	32	27.6%	7	58.3%	

Among 128 children in the study 122 had no oral thrush and 6 had oral thrush among 122 who had no thrush 9 were positive and among 6 with oral thrush 3 were positive. This was statistically significant.

Oral thrush	Elisa status				Chi square
	Negative		Positive		
	n	%	n	%	X2=12.2
No	113	97.4%	9	75%	p=0.001 **significant**
Yes	3	2.6%	3	25%	

Among 128 children 107 had no generalised lymphadenopathy and 21 had generalised lymphadenopathy. Among 107, 7 were positive and among 21 5 were positive. This was statistically significant.

GLA	Elisa status				Chi square
	Negative		Positive		
	n	%	n	%	X2=6.16
No	100	86.2%	7	58.3%	p=0.001 **significant**
Yes	16	13.8%	5	41.7%	

Taking in to account oral thrush and wasting as one group among 128 children 84 had neither oral thrush nor wasting and 44 had either wasting or oral thrush and sensitivity and specificity both increased when both were taken as one group

Oral thrush and wasting	Elisa status				Chi square
	Negative		Positive		
	n	%	n	%	X2=6.12
No	80	95.2%	4	4.8%	p=0.01 **significant**
Yes	36	81.8%	8	18.2%	

This prospective study enrolled 128 children(77 boys; 51 girls m:f 3:2) aged 0-12 yrs mean age of study population was 45.43 ± 36.776 months maximum number of children were in the age group of 1.5-5yrs (49,38.3%). Wasting was the commonest sign noted in the children enrolled (39, 30.5%) followed by hepatosplenomegaly (32, 25.2%).

None of the children had LIP, Esophageal candidiasis, PCP, HIV encephalopathy. Provisional diagnosis at the time of admission were TB, Pnuemonia, Acute Gastro Enteritis , probable immunodeficiency, typhoid, malaria, leukemia, lymphoma, PEM, etc.

RELATIONSHIP BETWEEN RISK FACTOR AND HIV POSITIVITY

In study population 12 children were found to be positive (9.3%).

Seropositivity rate of various manifestations varied from 8.3 % for persistent pneumonia, 16.7 % for Hepatosplenomegaly, 25 % for oral thrush, 41.7 % for GLA and 58.3 % for wasting. As noted , oral thrush, wasting and generalized lymph adenopathy were significant clinical risk factors for

predicting HIV seroprevalence.Children with oral thrush had 17 times increased risk of being HIV positive compared to those who did not have thrush. Children with wasting have 3 times increased risk of being HIV positive compared to those who did not have wasting. Though hepatosplenomegaly was not a significant risk factor for HIV seropositivity ,Children with hepatosplenomegaly have 2 times greater risk of being seropositive than those without hepatosplenomegaly. Though generalized lymphadenopathy was a significant risk factor for HIV seropositivity ,Children with generalized lymphadenopathy have 2 times greater risk of being seropositive than those without generalized lymphadenopathy.Though lymphoma was not a significant risk factor for HIV seropositivity ,Children with lymphoma have 3 times greater risk of being seropositive than those without lymphoma.

Manifestations		ELISA STATUS				Chi square test
		Negative		Positive		
		n	%	n	%	
Previous BT	No	115	99.1%	11	91.7%	$\chi 2=3.95$ P=0.05
	Yes	1	0.9%	1	8.3%	**Significant**
GLA	No	100	86.2%	7	58.3%	$\chi 2=6.16$ P=0.001
	Yes	16	13.8%	5	41.7%	**Significant**
HSM	No	85	73.9%	10	83.3%	$\chi 2=0.51$P=0.47
	Yes	30	26.1%	2	16.7%	not significant
Persistant pnuemonia	No	97	83.6%	11	91.7%	$\chi 2=0.53$ P=0.46
	Yes	19	16.4%	1	8.3%	not significant
Multiple bacterial infection	No	99	91.4%	12	100.0%	$\chi 2=1.12$ P=0.28
	Yes	17	8.6%			not significant
Disseminated TB	No	105	91.3%	10	83.3%	$\chi 2=0.81$ P=0.37
	Yes	10	8.7%	2	16.7%	not significant
Prolonged fever	No	100	87.0%	12	100.0%	$\chi 2=1.77$ P=0.18
	Yes	15	13.0%			not significant
Chronic cough	No	114	98.3%	12	100.0%	$\chi 2=0.21$ P=0.65
	Yes	2	1.7%			not significant
Chronic diarrhea	No	112	98.3%	12	100.0%	$\chi 2=0.21$ P=0.65
	Yes	4	1.7%			not significant
Wasting	No	84	72.4%	5	41.7%	$\chi 2=4.85$ P=0.02
	Yes	32	27.6%	7	58.3%	**Significant**
Oral thrush	No	113	97.4%	9	75.0%	$\chi 2=12.2$ P=0.001
	Yes	3	2.6%	3	25.0%	**significant**
Generalized dermatitis	No	113	98.3%	12	100.0%	$\chi 2=0.21$ P=0.65
	Yes	2	1.7%			not significant
Recurrent common infection	No	108	93.1%	12	100.0%	$\chi 2=0.88$ P=0.64
	Yes	8	6.9%			not significant

DISCUSSION

HIV infection has become one of the greatest pandemic ever. Children are caught in the HIV epidemic as innocent by standers It is in the process of nullifying all the good works and achievements done in the field of child survival in the form of immunization, ARI control programme, Diarrhoea control programme, promotion of breast feeding. This determines a major set back to child health.

One of the problems in establishing the diagnosis in developing countries has been the lack of adequate lab facilities and fact that clinical manifestations of HIV infection in children are often seen in uninfected children[30]. There are few published reports of clinical manifestations in pediatric HIV infection in India.

At the same time undertaking workup for the diagnosis of HIV infection means spending of community's precious resources[31]. Although antibody based tests for diagnosis are comparitively inexpensive, the cost involved in associated process of counseling can be enormous. Counselling is also considered to be time consuming and is emotionally draining on the staff[32.]

Routine HIV testing is not a feasible option considering the economical and psychological cost involved. Clinically directed selective screening is the only way out to achieve the dual objective of diagnosing the maximum number of subjects without wasting resources in undue manner.

In our study, the overall seropositivity rate was 9.3 %. This rate cannot be considered to reflect seropositivity rate in population not even in children. It

could be much lower. The rate found in this study indicates that selectively directed screening has been abled to facilitate diagnosis of HIV infection in hospitalized children.

We selected several risk factors that included common clinical features seen in admitted children (prolonged fever, severe malnutrition, persistent cough, repeated common infection, generalized lymphadenopathy and hepatosplenomegaly), features that were considered highly specific for childhood HIV infection (Pnuemocystis Carnii Pnuemonia, chronic parotid swelling, recurrent bacterial infection) and features reported to be associated with higher seropositivity rate for HIV infection (chronic diarrhea, oral candidiasis, disseminated TB).

This study could not encounter single case of PCP, LIP, HIV encephalopathy. This indicates these signs are uncommon in admitted children whether HIV positive or otherwise.

AGE AT PRESENTATION

Study	Mean age at presentation
S.Bavadekar etal (2005)[31]	55 months
Daniel E.Alikor et al., (2006)[33]	84 months
Tahziba Hussain et al., (2004)[34]	42 months
R.Lodha et al., (1999)[3]	55 months
R.Dhurrat et al., (2000)[26]	38 months
R.Merchant et al ., (1997)[27]	38 months
This study.	45 months

In this study, mean age at presentation was 45 months which is close to that of study by Tahziba Hussain et al[34]. which showed 42 months as mean age at presentation, while others like R.Lodha et al.[3], Daniel E.Alikor et al[33].and S.Bavadekar et al[31] showed higher age at presentation and R.Dhurrat et al[26] and R.Merchant et al [27]., showed lower age at presentation. This may be due to varied age at presentation in different communities. The study could not find any correlation between seropositivity for HIV and age at presentation. However the selected manifestations were 56% sensitive and 58% specific between age groups of 31 to 34 months in this study.

SEX

Study	Significance
Tahziba Hussain et al., (2004)[34]	Significantly higher in males than females
S.Bavadekar etal (2005)[31]	No significant statistical difference between gender
R.Dhurrat et al., (2000)[26]	No significant statistical difference between gender
Daniel E.Alikor et al., (2006)[33]	No significant statistical difference between gender
This study	No significant statistical difference between gender

The study showed no significant statistical difference in seroprevalence for HIV between gender. This was supported by studies like S.Bavadekar etal (2005)[31],R.Dhurrat et al., (2000)[26],Daniel E.Alikor et al., (2006)[33] while Tahziba Hussain et al., (2004)[34] found HIV infection was significantly higher in male children (82%) than female children (18%) when found along with TB. This may be due to higher prevalence of TB in males.

PARENT OCCUPATION

FATHER'S OCCUPATION

This study could not find any correlation between father's occupation and ELISA positivity in children. Most of the fathers were laborer by occupation (84, 65%) followed by mason (11, 8%).

Rodriquer B and Steil Duncan et al., (2004)[35] also showed that majority of fathers of HIV positive children whose occupation were known to semi skilled or unskilled labors .

Kristi mman et al., 2005, showed agricultural occupation was most common among fathers of children who were seropositive for HIV. This higher incidence of HIV among the children of semikilled, unskilled and agricultural laborers may be attributed to their lack of knowledge and awareness in the aspects of modes of transmission and prevention of HIV.

MOTHERS OCCUPATION

Among the mothers of children enrolled in the study, only 19 (14%) were working women, mostly getting daily wages. Rest others were house wives. All the mothers of ELISA positive children in this study were house wives and it was statistically significant. As the fathers' ELISA status of all the children who were seropositive for HIV in this study was not known, no comment can be made on the infective partner. Also HIV status statistics of both working women and house wives in our setup is not available and hence this statistical significance of mothers' occupation status can be ignored.

PARENT'S HIV STATUS

In this study there was no correlation between HIV status of parents with child's HIV positivity. Tahziba Hussain et al., (2004)[34] showed 80% of children with HIV positivity had either father or mother HIV positive. R.Lodha et al., (1999)[26] showed that all the fathers of children who were seropositive were seronegative for HIV while few of mothers were elisa positive. P Parthasarathy et al[36] showed 22% of seropositive children had either father or mother positive

HISTORY OF PREVIOUS BLOOD TRANSFUSION

This study showed statistically significant correlation between blood transfusion and seropositivity. R.Lodha et al., (1999)[3] also showed contaminated blood transfusion seems to be a source of infection for HIV in children in New Delhi and all the transfusions were given for poorly defined conditions. R.Dhurrat et al., (2000)[26] found higher incidence of HIV among thalassemic children who were given multiple blood transfusions. R.Merchant et al ., (1997)[27] however found that blood transfusion was not a significant risk factor.All these studies state that blood transfusion continues to be a significant risk factor for HIV transmission. So children should be given blood transfusion only under well defined conditions with utmost safety precautions. Though PCR can detect the presence of HIV infection in the window period, it cannot be routinely used for screening of blood products considering its cost.

SYMPTOM ANALYSIS

ORAL THRUSH

STUDY	PERCENTAGE
S.Bavadekar etal (2005)[31]	75%
R.Lodha et al., (1999)[3]	36%
R.Dhurrat et al., (2000)[26]	50%
R.Merchant et al ., (1997)[27]	14%
Karande et al., (2002)37	80%
I.shah et al .,(1994)[38]	14%
I. E.Modi et al., (1989)[39]	19%
This study.	25%

This study found that oral thrush is a single significant identifiable risk factor for HIV. None of the studies mentioned here have contradicted the above finding.

WASTING SYNDROME

STUDY	PERCENTAGE
S.Bavadekar etal (2005)[31]	50%
R.Lodha et al., (1999)[3]	100%
R.Dhurrat et al., (2000)[26]	48%
R.Merchant et al ., (1997)[27]	45%
Tovo et al .,(1992)[40,41]	50%
Greenberg et al., (1998)[42]	90%
Italian register for HIV in Children (1994) [43]	78%
This study	60%

In the present study wasting syndrome (failure to thrive, Grade III and Grade IV PEM) was the other significant identifiable risk factor for HIV other than oral thrush and GLA. This finding is supported by all the other studies. R.Lodha et al., showed that wasting was a risk factor in all the children in their study.

GENERALISED LYMPHADENOPATHY

STUDY	PERCENTAGE
S.Bavadekar etal (2005)[31]	50%
R.Lodha et al., (1999)[3]	40%
R.Dhurrat et al., (2000)[26]	35%
R.Merchant et al ., (1997)[27]	23%
Tovo et al .,(1992)[40,41]	78%
Greenberg et al., (1998)[42]	91%
Italian register for HIV in Children (1994)[43]	91%
I.shah et al .,(1994)[38]	26%
I. E.Modi et al., (1989)[39]	60%
This study.	41.7%

HEPATOSPLENOMEGALY AS A RISK FACTOR

STUDY	PERCENTAGE
R.Dhurrat et al., (2000)[26]	67%
R.Merchant et al ., (1997)[27]	30%
I.shah et al .,(1994)[38]	30%
S,R.Daga et al., [30]	30%
This study	16%

The lower incidence of HIV seropositivity in patients with hepatosplenomegaly in this study may be due to other diseases like malaria, typhoid, dengue, hepatitis, cirrhosis of liver etc., that present with hepatosplenomegaly are more prevalent in our area.

EXTRA PULMONARY TUBERCULOSIS

Study	Percentage
P.Parthasarathy et al[36]	6%
S.Bavadekar et al[31]	20%
S.R.Daga et al[30]	33%
R.Dhurrat et al[26]	67%
I.Shah et al[38]	30%
R.Merchent et al[27]	30%
Tazhiba hussain et al[34]	13%
This study	16%

The present study showed seroprevalance of 16% with extra pulmonary TB.

Tuberculosis is a common problem among children with HIV. The high prevalence of tuberculosis among HIV-infected adults leads to increased risk of this infection among infected children. Therefore it is essential to monitor these children carefully and institute treatment early, since response to treatment is good. Since tuberculin test may be negative in a significant proportion of these children, one must be careful not to relay solely on this test for screening.

R.merchent et al., found tuberculosis is one of the most common life threatening opportunistic infections among children infected with HIV, and it occurs at higher CD4 cell counts when immune deficiency is comparatively less advanced Studies from Zambia show that HIV seroprevalence rate is 37% amongst children with tuberculosis as compared to 11% amongst those without TB.HIV seropositivity was 53% in 12-18 month age group and 14% in 10-14 yrs old. Unfortunately similar studies from India are lacking. However as the disease pattern and socio economic conditions are similar to those in Africa the alarmingly high HIV seroprevalence in this study can be explained. Tazhiba Hussain et al., showed 13% incidence of HIV among TB patients in pediatric age group. 82% of TB patients had a history of positive contact i.e., one of the parent were HIV affected. The lower prevalence found in the present study is more likely to be the result of different selection criteria.

PERSISTANT PNUEMONIA:

Study	Percentage
R.Dhurrat et al.,[26]	24%
I.Shah et al.,[38]	32%
R.Merchent et al.,[27]	32%
I.J.EModi et al.,[39]	32%
R.Lodha et al.,[3]	16%
This study	8.3%

This lower incidence of HIV as a cause of persistent pneumonia could be explained by more common cause like pulmonary TB or foreign body in our setup.

RECURRENT BACTERIAL INFECTION

Study	Percentage
S.R.Daga et al., 1999[30]	26%
Tovo et al.,1992 [40,41]	12%
Greenberg et al., (1999)[42]	41%
Italian register for HIV in Children (1994)[43]	26%
This study	0%

Our study showed no correlation between the seropositivity for ELISA and recurrent bacterial infections.

S.Bavadekar et al., (2005) also supported this study by finding no correlation between recurrent bacterial infection and seropositivity for ELISA.

While all other studies were against our finding with respect to recurrent bacterial infection, this could be due to varied incidence of RBI in different countries.

PROLONGED FEVER

Study	Percentage
S.Bavadekar et al[31]	18 %
I.Shah et al[38]	12 %
Tovo et al.,1992 [40,41]	43 %
Greenberg et al., (1999)[42]	85 %
Italian register for HIV in Children (1994)[43]	71 %
I.J.Emodi[39]	51 %
R.Lodha et al.,[3]	95 %
This study	0 %

In this present study none of the children with prolonged fever were seropositive for HIV. This could be due to the fact that in our setup there were various other conditions which present with prolonged fever such as malaria,

urinary tract infection, TB etc., hence there is no need in routinely screening children with prolonged fever for HIV until all other investigations are negative.

CHRONIC DIARRHEA

Study	Percentage
Italian register for HIV in children[43]	50%
Tova et al[40,41]	30%
R.Lodha et al[3]	45%
S.R .Daga et al[30]	42%
R.Dhurrat et al[26]	30%
R.Merchent et al[27]	24%
I.J.Emodi et al[39]	38%
Parthasarathy et al[36]	4%
The present study	none

The present study could not find any correlation between chronic diarrhea and seropositivity for HIV**.** S.Bavadekar et al also found that chronic diarrhea was not a significant risk factor for child being seropositive for HIV

In our set up children are more top fed along with breast feeding that too mostly with feeding bottles, and our area is surrounded by slums with poor sanitation facilities and very poor hygiene this could explain the higher

incidence of chronic diarrhea in our set up with out the child being seropositive for HIV

E.Sami et al 1994 [44]showed that diarrhoea lasting for more than 14 days is a risk factor for child being sero positive for HIV

CHRONIC OR PERSISTENT COUGH

I.J.Emodi et al[39] showed 32%, R.Lodha et al[3] showed 86% association of chronic cough with HIV. The present study could not find any correlation between presence of chronic cough an elisa positivity for HIV

S.Bavadekar et al also found no correlation between presence of chronic cough and elisa positivity for HIV. This could be due to the fact that TB was more prevalent in our setup and bronchial asthma was other cause of chronic cough in our set up

CHRONIC PAROTITIS

R.Dhurrat et al[26] found 13% seropositivity rate for HIV amongst children with chronic parotitis.R.Merchent et al.,[27] and I.Shah et al[38] found lower seroprevalence in children with chronic parotitisThe present study enrolled two children with chronic parotitis but both were sero negative for HIV. both were referred as partially treated mumps to us.S.Bavadekar et al also found no cases of chronic parotitis.This may be due to the fact that chronic parotitis is rare in children whether HIV positive or otherwise

GENERALIZED DERMATITIS

Study	Percentage
S.Bavadekar et al[31]	83%
I.J.Emodi et al[39]	37%
R.Dhurrat et al[26]	31%
I.Shah et al[38]	22%
S.R.Daga et al[30]	10%
The present study	None

The present study could not find many cases of generalized dermatitis other than two cases of recurrent herpes zoster and both were seronegative for HIV

CONCLUSION

1. The present study found a overall prevalence rate of 9.3% for HIV amongst hospitalized children when they are admitted with at least one of selected manifestations

2. The study found oral thrush, generalized lymphadenopathy and wasting were single significant risk factor for child being sero positive for HIV

3. On considering oral thrush an wasting as one group sensitivity and specificity increased

4. The study found that, prolonged fever ,persistent pneumonia,chronic cough,chronic diarrhea,recurrent bacterial infection were not the significant risk factors for child being sero positive for HIV

5. Selected manifestations were 58% sensitive and 56% specific between the age groups of 31-34 months

6. There was no correlation between parent occupation or elisa status and child's sero positivity

7. There was no correlation between gender child's sero positivity

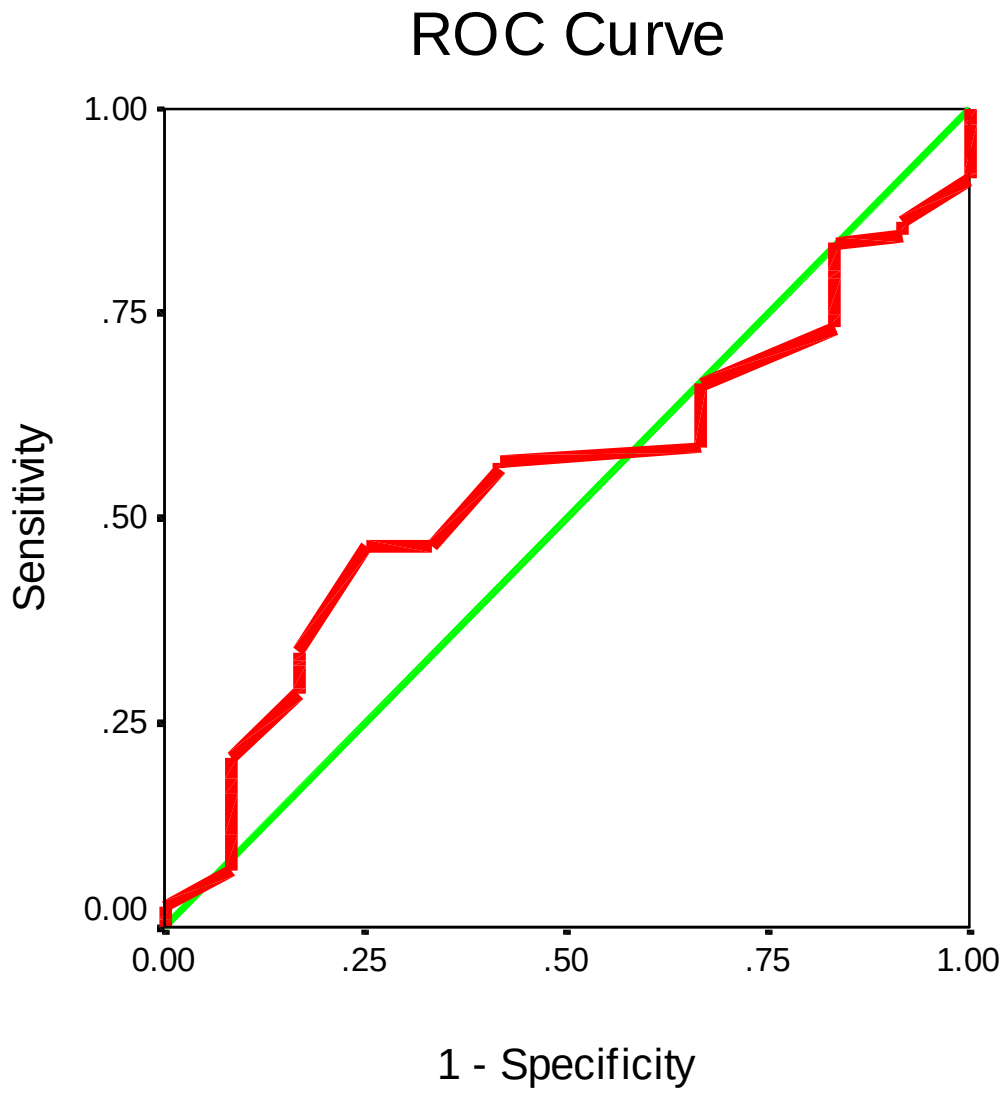
MASTER CHART

S.No.	AGE	SEX	F.Occ.	M.Occ.	HIV (M)	HIV (F)	PREV BT	GLA	HSM	PER. PNEU	MBI.	EP TB	FEVER	COUGH	CHR. DIARR	WASTING	ORAL THR	RBI	GENDER	ELISA STATUS
1	108	2	MASON	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
2	48	1	FARMER	HW	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1	2
3	72	2	FARMER	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
4	72	1	COOLEY	HW	0	0	1	1	0	0	0	0	0	0	0	1	0	0	0	1
5	48	1	COOLEY	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1
6	42	1	COOLEY	HW	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	1
7	72	1	COOLEY	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
8	18	2	COOLEY	HW	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	1
9	72	2	COOLEY	HW	0	0	0	0	1	0	0	0	0	0	1	1	0	0	0	2
10	24	1	COOLEY	HW	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2
11	36	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
12	66	1	MASON	HW	1	1	0	0	1	0	0	0	1	0	0	0	0	0	0	2
13	84	1	FISHMAN	HW	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	2
14	24	1	STEEL POLISHER	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
15	30	1	MASON	HW	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	1
16	12	1	MASON	HW	0	0	0	0	0	1	0	0	0	0	0	0	1	1	0	2
17	96	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
18	120	1	COOLEY	HW	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	2
19	108	2	COOLEY	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
20	18	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
21	24	2	TAILOR	HW	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	2
22	144	2	BARBER	HW	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2
23	18	1	TAILOR	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	2
24	30	2	SALESMAN	HW	0	0	1	1	0	1	0	0	0	0	0	1	0	0	0	2
25	18	2	COOLEY	HW	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	2
26	36	1	DRIVER	HW	1	0	0	0	0	0	0	0	1	0	0	1	0	1	0	2
27	96	1	COOLEY	HW	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2
28	48	2	COOLEY	HW	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	2
29	72	2	SHOP OWNER	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0	2
30	30	1	SHOP OWNER	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
31	120	1	PAINTER	HW	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	2

S.No.	AGE	SEX	F.Occ.	M.Occ.	HIV (M)	HIV (F)	PREV BT	GLA	HSM	PER. PNEU	MBI.	EP TB	FEVER	COUGH	CHR. DIARR	WASTING	ORAL THR	RBI	GENDER	ELISA STATUS
32	9	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
33	6	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
34	9	1	FISHMAN	HW	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	2
35	15	1	FISHMAN	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
36	48	2	COOLEY	HW	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	2
37	72	1	DRIVER	HW	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	2
38	84	1	COOLEY	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
39	48	1	COOLEY	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
40	36	1	COOLEY	HW	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
41	36	2	COOLEY	HW	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
42	132	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
43	36	1	COOLEY	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
44	120	2	COOLEY	HW	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	2
45	4	1	COOLEY	HW	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
46	24	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
47	48	1	STEEL POLISHER	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
48	7	2	COOLEY	HW	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
49	8	2	STEEL POLISHER	HW	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	2
50	108	1	COOLEY	HW	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	2
51	12	1	COOLEY	COOLEY	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
52	48	1	COOLEY	HW	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	2
53	108	1	COOLEY	COOLEY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
54	4	1	TAILOR	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
55	3	1	STEEL POLISHER	HW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
56	132	1	COOLEY	HW	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	2
57	18	1	FARMER	HW	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
58	36	1	PAINTER	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
59	4	1	STEEL POLISHER	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
60	6	1	COOLEY	COOLEY	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	2
61	120	1	COOLEY	COOLEY	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
62	7	1	COOLEY	COOLEY	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
63	48	2	FARMER	HW	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2

S.No.	AGE	SEX	F.Occ.	M.Occ.	HIV (M)	HIV (F)	PREV BT	GLA	HSM	PER. PNEU	MBI.	EP TB	FEVER	COUGH	CHR. DIARR	WASTING	ORAL THR	RBI	GENDER	ELISA STATUS
64	36	2	COOLEY	HW	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
65	4	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
66	48	1	COOLEY	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
67	24	2	COOLEY	HW	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	2
68	3	1	COOLEY	HW	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
69	8	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
70	5	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
71	6	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
72	60	1	TAILOR	HW	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2
73	30	2	DRIVER	HW	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	1
74	60	2	COOLEY	COOLEY	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	2
75	120	2	MASON	HW	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
76	48	1	TEA VENDOR	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
77	72	1	COOLEY	COOLEY	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	2
78	84	1	FISHERMA	HW	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	2
79	9	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
80	4	1	DRIVER	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
81	108	1	CARPENTER	COOLEY	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2
82	48	1	COOLEY	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
83	6	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1
84	10	1	COOLEY	HW	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	2
85	36	1	COOLEY	COOLEY	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	2
86	18	1	COOLEY	HW	0	0	0			0	0	0	0	0	0	1	0	0	0	2
87	48	2	MASON	HW	0	0	0	0	0	0	1		0	0	0	0	0	1	0	2
88	24	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
89	36	1	COOLEY	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
90	96	2	COOLEY	HW	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	2
91	48	1	COOLEY	HW	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2
92	12	1	MASON	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
93	60	2	COOLEY	COOLEY	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
94	72	2	DRIVER	COOLEY	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	2
95	6	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
96	48	2	COOLEY	HW	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	2
97	36	1	COOLEY	COOLEY	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	2
98	30	1	COOLEY	HW	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	1

S.No.	AGE	SEX	F.Occ.	M.Occ.	HIV (M)	HIV (F)	PREV BT	GLA	HSM	PER. PNEU	MBI.	EP TB	FEVER	COUGH	CHR. DIARR	WASTING	ORAL THR	RBI	GENDER	ELISA STATUS
99	4	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
100	9	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
101	48	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
102	72	1	COOLEY	COOLEY	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
103	12	2	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
104	32	1	MASON	HW	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
105	24	1	COOLEY	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
106	120	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
107	96	1	TAILOR	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
108	52	2	COOLEY	HW	0	0	0	0	0	0	0	0		0	0	0	0	0	0	2
109	18	1	MASON	COOLEY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
110	72	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2
111	6	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
112	48	2	COOLEY	HW	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2
113	96	2	COOLEY	COOLEY	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	2
114	18	2	COOLEY	HW	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2
115	24	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
116	4	1	MASON	HW	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	2
117	90	2	COOLEY	HW	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	2
118	18	1	COOLEY	HW	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	2
119	36	2	FISHERMAN	HW	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2
120	96	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2
121	12	2	COOLEY	COOLEY	0	0	0	0	0	0	0	0	1	0	0	1	0		0	2
122	54	2	TAILOR	HW	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	2
123	24	1	COOLEY	HW	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	2
124	90	1	COOLEY	COOLEY	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
125	6	1	COOLEY	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2
126	36	2	COOLEY	HW	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	2
127	18	2	COOLEY	HW	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
128	15	1	MASON	HW	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2


ROC Curve
Sensitivity
1.00
.75
.50
.25
0.00
0.00
.25
.50
.75
1.00
1 - Specificity